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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/479,997	06/07/95	ENGELHARDT D	ENZ-5(D6)(C2

HM12/0718

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EXAMINER	
HOUTTEMAN, S	
ART UNIT	**PAPER NUMBER**
1656	34

DATE MAILED: 07/18/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/479,997	Engelhardt et al.
Examiner	**Group Art Unit**
Scott Houtteman	1656

☒ Responsive to communication(s) filed on *6/20 and 6/23, 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *454-575* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *454-575* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Applicant's response, filed 6/20/00 and letter filed 6/23/00, has been carefully considered with the following effect:

The objections and rejections of the previous Office action mailed 2/3/99, have been maintained.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 459-472 and 474-575 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record. This is a "new matter" rejection.

Support was not found were indicated in the specification, nor elsewhere, for the following limitations in Claims 459-472 and 474-575:

Claims 459-463, specific chemical compositions of linkages;

Claims 464-472, 482-569, specific identity of labels and points of attachment of the "SIG" moiety to internal phosphates;

Claims 474-477 and 570-575, the "composition" limitation, in addition to the above identified limitations.

4. Claims 454-575 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record.

Halloran et al., J. Immunol. 96(3):373-378, 1966 (Halloran) discloses the attachment of a specific signal moiety, a protein, to the phosphorus atom of the phosphate moiety using a specific linker, a -C-$(CH_2)_4$-N- chain. In contrast, the claims are drawn to a much broader category, a generic "SIG" moiety and linkage, and specific compounds such as those recited in claim 464 -- magnetic, hormone, metal containing "SIG" moieties, for example.) Thus, the scope of the enablement is not commensurate with the scope of the claims.

In addition, several of the reference articles are drawn to labeling a mononucleotide and express doubt about labeling an oligonucleotide. Armstrong et al., Eur. J. Biochem. 0:33-38, 1976, teaches that the labeled mononucleotides are "strong competitive inhibitors" of the reaction which is necessary to produce a labeled oligonucleotide from a labeled mononucleotide. See Armstrong, p. 33, col. 1. This reaction is the use of the labeled mononucleotide as a substrate for the polymerase mediated synthesis of the oligonucleotide.

While Armstrong teaches that some labeled mononucleotide will be incorporated, Armstrong teaches no guidance as to which of the myriad labels within the scope of these claims will function in the claimed invention. Lacking any guidance in the specification and in view of the breadth of the claims, it would require undue experimentation in order to enable a reasonable number of embodiments of these claims. The skilled artisan would have to experiment with

various SIG moieties, linkages and attachment sites, as well as various reaction protocols and protecting groups.

5. Claims 454-575 are rejected under 35 U.S.C. § 103 for being unpatentable over Gohlke et al., US Patent 4,378,458, 3/1983, filed 3/1981 (Gohlke) in view of Sodja et al., Nucleic Acids res., 5(2):385-401, 1978 (Sodja) and further in view of applicant's admissions for reasons of record.

6. Claims 454-575 are rejected under 35 U.S.C. § 103 for being unpatentable over Halloran et al., J. Immunol. 96(3):373-378, 1966 or Miller et al. 20(7):1874-1880, 1981 for reasons of record.

Both Halloran and Miller teach specific labels, (SIG moieties such as proteins and thiophosphates) attached to nucleic acids. See Halloran p. 373, Fig. 1 and col. 2; Miller p. 1874, col. 1. These prior art references differ from the claims in the recitation of some specific labels and linkages. It would have been *prima facie* obvious, however, to one of ordinary skill in the art at the time the invention was made to substitute any linker or label in the methods of Halloran and Miller for the expected benefit of constructing multiple labels. Given the fact that diverse labels such as proteins and thiophosphates, the ordinary artisan would have reasonably expected any moiety used as a label to function in the claimed invention.

7. Repeating an important point from a previous Office action, applicants arguments to the 35 U.S.C. § 112, first paragraph rejections have provided strong evidence of obviousness and vice-versa. For example, the references used to support enablement, Halloran and Miller add evidence of obviousness.

It is important that the arguments for patentability explain, that the prior art supplied by applicant, for example Halloran and Miller, can buttress the specification--providing needed evidence that the thin "SIG Phosphate" disclosure both "describes" and "enables" the detailed invention now claimed--but that these same prior art references do not render the claims obvious.

Furthermore, the criticisms of the obviousness rejections must be made without undermining the enablement rejection. For example, if arguing that Halloran and Miller are somehow "non-enabled" one must justify how the specification can be enabled. After all, the prior art contains much more detail than that found in the specification.

Finally, the specification is held to a higher standard than the teachings of the prior art supplied in an obviousness rejection. As stated in a previous office action:

> 35 U.S.C. § 112 provides that, in return for the grant of monopoly, the specification must enable one skilled in the art to "make and use" the invention without "undue experimentation" whereas 35 U.S.C. § 103 makes no such requirement. Thus, a teaching of how to use a compound can be entirely adequate to render a claim obvious but, at the same time, entirely inadequate to support the allowance of such a claim.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

9. Papers relating to this application may be submitted to Technology Center 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Technology Center 1600 Fax numbers are (703) 305-3014 and 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott Houtteman whose telephone number is (703) 308-3885. The examiner can normally be reached on Tuesday-Friday from 8:30 AM - 5:00 PM. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center receptionist whose telephone number is (703) 308-0196.

Scott Houtteman
July 17, 2000

Scott W. Houtteman

SCOTT W. HOUTTEMAN
PRIMARY EXAMINER